ORIGINAL ARTICLE

A Comparison of Laparoscopically Assisted and Open Colectomy for Colon Cancer

The Clinical Outcomes of Surgical Therapy Study Group*

ABSTRACT

BACKGROUND

Minimally invasive, laparoscopically assisted surgery was first considered in 1990 for patients undergoing colectomy for cancer. Concern that this approach would compromise survival by failing to achieve a proper oncologic resection or adequate staging or by altering patterns of recurrence (based on frequent reports of tumor recurrences within surgical wounds) prompted a controlled trial evaluation.

METHODS

We conducted a noninferiority trial at 48 institutions and randomly assigned 872 patients with adenocarcinoma of the colon to undergo open or laparoscopically assisted colectomy performed by credentialed surgeons. The median follow-up was 4.4 years. The primary end point was the time to tumor recurrence.

RESULTS

At three years, the rates of recurrence were similar in the two groups — 16 percent among patients in the group that underwent laparoscopically assisted surgery and 18 percent among patients in the open-colectomy group (two-sided P=0.32; hazard ratio for recurrence, 0.86; 95 percent confidence interval, 0.63 to 1.17). Recurrence rates in surgical wounds were less than 1 percent in both groups (P=0.50). The overall survival rate at three years was also very similar in the two groups (86 percent in the laparoscopic-surgery group and 85 percent in the open-colectomy group; P=0.51; hazard ratio for death in the laparoscopic-surgery group, 0.91; 95 percent confidence interval, 0.68 to 1.21), with no significant difference between groups in the time to recurrence or overall survival for patients with any stage of cancer. Perioperative recovery was faster in the laparoscopic-surgery group than in the open-colectomy group, as reflected by a shorter median hospital stay (five days vs. six days, P<0.001) and briefer use of parenteral narcotics (three days vs. four days, P<0.001) and oral analgesics (one day vs. two days, P=0.02). The rates of intraoperative complications, 30-day postoperative mortality, complications at discharge and 60 days, hospital readmission, and reoperation were very similar between groups.

CONCLUSIONS

In this multi-institutional study, the rates of recurrent cancer were similar after laparoscopically assisted colectomy and open colectomy, suggesting that the laparoscopic approach is an acceptable alternative to open surgery for colon cancer.

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Minimally invasive surgery revolutionized the way operations were performed. Gallbladder procedures that previously required long incisions and extended periods of hospitalization were transformed through the use of laparoscopic techniques.[1,2] The possibility that this approach could benefit patients undergoing colectomy for colon cancer was first considered in 1990.[3] However, a number of cancer-specific questions arose, including the following: Could minimally invasive surgery achieve a proper oncologic resection, with the same extent of exploration and information about lymph-node staging provided by a standard open resection? Were patterns of tumor-cell dissemination altered or enhanced by the use of laparoscopic techniques? These concerns increased when high rates of tumor recurrence at wound and trocar sites were reported with the use of laparoscopy.

In 1994, in a series of laparoscopically assisted resections of colon cancer, 3 of 14 patients had tumor recurrence at the sites of trocar wounds.[4] As compared with a tumor-recurrence rate of less than 1 percent at the wound sites for open surgery,[5] the rates of 1 percent[6] to 21 percent[4] reported for laparoscopically assisted surgery provided a compelling rationale for a controlled evaluation.[7] In 1994, a prospective, randomized trial comparing laparoscopically assisted and open surgery for curable colon cancer was begun in multiple, diverse, surgical practices.[8] We report the first outcomes of cancer from that trial.

METHODS

PATIENTS

The details of the design and methods for this noninferiority trial have been reported previously.[8-10] Inclusion criteria were a clinical diagnosis of adenocarcinoma of the colon (histologic confirmation was required at surgery), an age of at least 18 years, and the absence of prohibitive abdominal adhesions. Exclusion criteria included advanced local or metastatic disease, rectal or transverse colon cancer, acute bowel obstruction or perforation from cancer, and severe medical illness. Inflammatory bowel disease, familial polyposis, pregnancy, or concurrent or previous malignant tumor also precluded enrollment. The study was approved by the institutional review board of each participating center, and all patients provided written informed consent.

SURGICAL PROCEDURES AND QUALITY CONTROL

Participation in this trial was limited to 66 credentialed surgeons at 48 institutions. Each surgeon had performed at least 20 laparoscopically assisted colorectal operations. Surgeons submitted a videotape of a laparoscopically assisted colectomy that was reviewed to assess their oncologic technique, including the level of mesenteric ligation, the degree of avoidance of direct handling of the tumor, the identification of critical adjacent structures, and the thoroughness of abdominal exploration. Ongoing quality control included a random audit of videotapes and an assessment of bowel margins; both were reviewed by an external monitoring committee.

All laparoscopically assisted and open colectomies were performed according to protocol guidelines, with the same extent of resection for both groups. For laparoscopically assisted resections, a pneumoperitoneal and an intracorporeal approach were used to explore the abdomen, mobilize the colon, identify critical structures, and ligate the vascular pedicle for left-sided and sigmoid colectomies. The bowel was exteriorized through a small incision for resection and anastomosis. Conversion from laparoscopically assisted to open surgery was allowed at the surgeon's discretion for the patient's safety and because of technical difficulties, the presence of associated conditions, or findings of advanced disease or inadequate oncologic margins.

Postoperative care, including early feeding and narcotic use, was according to the surgeon's standard practice. Adjuvant postoperative chemotherapy was allowed at the physician's or patient's discretion.

RANDOMIZATION

Randomization was performed centrally at the statistical office of the North Central Cancer Treatment Group. Through the use of a minimization algorithm,[11] the treatment assignment was balanced with respect to three stratification variables: site of the primary tumor (left side, right side, or sigmoid), American Society of Anesthesiologists class (class I, patient appeared healthy; class II, patient had systemic, well-controlled disease; or class III, patient had multiple symptoms of disease or well-controlled major system disease),[12] and surgeon. Patients were randomly assigned to undergo either open laparotomy and colectomy or laparoscopically assisted colectomy.

FOLLOW-UP

Patients were assessed for complications at the time of hospital discharge and at 2 and 18 months. Complications were assessed by a single reviewer who was unaware of patients' treatment assignments and were classified as follows: grade 1, non–life-threatening and temporary; grade 2, potentially life-threatening but temporary; grade 3, causing permanent disability; and grade 4, fatal.[13] Patients were evaluated for tumor recurrence as follows: physical examination, including checking for tumor recurrence at wound sites, and carcinoembryonic antigen testing every three months for the first year and then every six months for five years; chest radiography, every six months for two years and then annually; and colon evaluation, including colonoscopy or proctosigmoidoscopy and colon radiography, every three years. Confirmation of recurrence required imaging or pathological evaluation. Measures of the postoperative quality of life were collected and have been reported previously.[9]

STATISTICAL ANALYSIS

The primary end point was the time to tumor recurrence, defined as the time from randomization to the first confirmed recurrence. Patients who died without a reported tumor recurrence were assumed to have had a recurrence at death unless it was clearly documented otherwise, in which case the patient's data were censored on the date of death in the analysis of the time to recurrence. The primary analysis consisted of a one-sided log-rank test comparing time to recurrence in the two randomized groups. A one-sided P value of less than 0.09 in favor of open colectomy would result in the open-colectomy group's being declared superior; otherwise, the recurrence rate would be deemed not significantly worse with the laparoscopic procedure. On the basis of an accrual goal of 1200 patients, if the hazard ratio for recurrence with the laparoscopic procedure, as compared with the open procedure, was 1.23, there was an 81 percent chance of declaring the laparoscopic procedure inferior; if the hazard ratio was 1.0, there was a 9 percent chance of declaring the laparoscopic procedure inferior. This calculation assumed that there was a three-year recurrence-free rate of 80 percent among patients treated with open colectomy and a 21 percent rate of conversion from laparoscopically assisted to open colectomy and that patients whose procedures were converted would have the same recurrence rate as those assigned to undergo open colectomy.

The protocol included a specific plan for modifying the analysis if accrual was less than complete. This consisted of adjusting the significance value for the log-rank test, on the basis of the actual number of recurrences in the open-colectomy group, to retain an 81 percent chance of declaring the laparoscopic procedure inferior if it was associated with an increase of 23 percent in the risk of recurrence. Comparative efficacy data were not considered in this modification. In addition, this protocol was monitored by an external data-monitoring committee that reviewed and approved the final analysis plan. On the basis of the observed number of recurrences, the cutoff used for this analysis was 0.41. That is, if the one-sided P value in favor of the open procedure was less than 0.41, the open procedure would be declared superior; otherwise, the laparoscopic procedure would be declared not significantly worse.

Secondary end points included disease-free survival, overall survival, complications, variables related to recovery, and the quality of life. All eligible patients for whom surgery was attempted were included in the analyses except for those with benign pathological conditions, who were excluded from analyses of the time to recurrence, disease-free survival, and overall survival. Five patients assigned to the open-colectomy group underwent laparoscopically assisted surgery; these patients were included in the laparoscopic-surgery group for analysis to prevent the results from being biased toward noninferiority. Univariate comparisons of surgical and postoperative data were conducted with the use of a two-sample t-test for continuous data and a χ^2 test for categorical data.

Cumulative-incidence methods were used to estimate the rate of tumor recurrence.[14] Kaplan–Meier curves were used to estimate the distribution of disease-free and overall survival.[15] The log-rank test was used to compare time-to-event distributions[16]; the Cox proportional-hazards regression model was used for multivariate models.[17] Two sensitivity analyses for the time to recurrence, disease-free survival, and overall survival were conducted, one according to the intention to treat, which included all patients in their initially assigned groups, and a second that excluded patients who had stage IV disease at surgery. All reported P values were two-sided with the exception of a one-sided test for the primary analysis of the time to recurrence; P values of less than 0.05 were considered to indicate statistical significance.

RESULTS

CHARACTERISTICS OF THE PATIENTS AND TUMORS

Between August 1994 and August 2001, 872 patients underwent randomization (Fig. 1). Two patients declined to undergo any surgery and 7 were ineligible, leaving 863 patients for the final analysis. Among these patients, 53 had nonmalignant disease and 26 had stage IV disease identified at surgery (16 in the open-colectomy group and 10 in the group that underwent laparoscopically assisted colectomy). The two study groups were well balanced (Table 1). Only 14 patients (2 percent) revoked consent or were lost to follow-up (only 3 patients were lost to follow-up before four years).

SURGERY

A total of 428 patients underwent open colectomy, and 435 were treated initially with laparoscopically assisted colectomy. The procedure was converted to open colectomy for 90 patients assigned to laparoscopically assisted surgery (21 percent) (Table 2). Conversion rates did not differ significantly between surgeons with a high volume of procedures and those with a low volume or between surgeons who participated early or late in the trial (data not shown).

Operating times were significantly longer in the laparoscopic-surgery group than the open-colectomy group (150 minutes vs. 95 minutes, P<0.001). Patients in the open-colectomy group were more likely than those in the laparoscopic-surgery group to undergo concurrent resection of other organs (63 vs. 34 patients, P=0.001); malignant histologic findings were identified in these resected organs in 14 patients in the open-colectomy group, as compared with 6 in the laparoscopic-surgery group. Abdominal-wall adhesions (P=0.002) and bowel adhesions (P=0.001) were reported more frequently among patients in the laparoscopic-surgery group.

The extent of resection was similar in both groups; bowel margins were less than 5 cm in 6 percent of the patients in the open-colectomy group and 5 percent of those in the laparoscopic-surgery group (P=0.52). In each group, the median number of lymph nodes examined was 12.

RECOVERY AND COMPLICATIONS

Perioperative recovery was faster in the laparoscopic-surgery group than in the open-colectomy group, as reflected by a shorter hospital stay (P<0.001) and briefer use of parenteral narcotics (P<0.001) and oral analgesics (P=0.02) (Table 2). There were no significant differences between the groups in the rates of intraoperative complications (2 percent in the open-colectomy group and 4 percent in the laparoscopic-surgery group, P=0.10), 30-day postoperative mortality (P=0.40), rates and severity of postoperative complications at discharge (P=0.98) and at 60 days (P=0.73), and rates of readmission (10 percent and 12 percent, respectively; P=0.27), or the rates of reoperation (less than 2 percent in each group, P=1.0). The percentage of patients receiving chemotherapy did not differ significantly between groups and paralleled the rate of stage III disease.

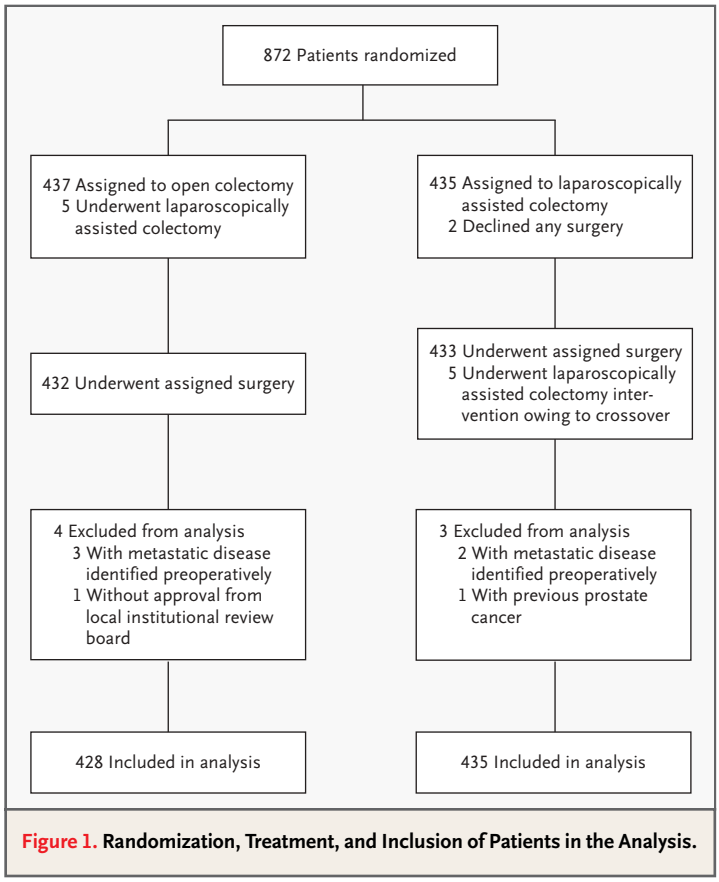

Figure 1. Randomization, Treatment, and Inclusion of Patients in the Analysis.

SURVIVAL AND RECURRENCE

After a median follow-up of 4.4 years, 160 patients had had a recurrence of tumor (84 in the open-colectomy group and 76 in the laparoscopic-surgery group) and 186 had died (95 and 91, respectively). Seventy-seven patients died before the tumor recurred (34 in the open-colectomy group and 43 in the laparoscopic-surgery group, P=0.25). The one-sided P value for the time to recurrence in favor of

Table 1. Baseline Characteristics of the Patients and Tumors.

Characteristic	Open Colectomy (N=428)	Laparoscopically Assisted Colectomy (N=435)
Age — yr		
Median	69	70
Range	29–94	28–96
Female sex — no. (%)	220 (51)	212 (49)
American Society of Anesthesiologists class — no. (%)		
1 or 2	367 (86)	373 (86)
3	61 (14)	62 (14)
Location of primary tumor — no. (%)		
Right side of colon	232 (54)	237 (54)
Left side of colon	32 (7)	32 (7)
Sigmoid colon	164 (38)	166 (38)
TNM stage — no. (%)*		
0	33 (8)	20 (5)
I	112 (26)	153 (35)
II	146 (34)	136 (31)
III	121 (28)	112 (26)
IV	16 (4)	10 (2)
Unknown	0	4 (1)
Depth of invasion — no. (%)		
Submucosal, not muscle wall	59 (14)	67 (15)
Muscle wall, not serosal or perirectal	76 (18)	105 (24)
Serosal	237 (55)	226 (52)
Beyond serosa or perirectal fat, involvement of contiguous structure	23 (5)	12 (3)
Not applicable (benign pathological findings)	33 (8)	20 (5)
Unknown	0	5 (1)
Grade of differentiation — no. (%)		
1 (Well)	44 (10)	36 (8)
2 (Moderately)	271 (63)	315 (72)
3 (Poorly)	72 (17)	51 (12)
4 (Undifferentiated)	6 (1)	5 (1)
Not applicable (benign pathological findings)	33 (8)	20 (5)
Unknown	2 (<1)	8 (2)
No. of previous operations — no. (%)		
0	233 (54)	246 (57)
1	120 (28)	113 (26)
>1	37 (9)	41 (9)
Unknown	38 (9)	35 (8)

* TNM denotes tumor–node–metastasis.

the open procedure was 0.83, satisfying the criteria to declare the laparoscopic procedure not significantly inferior to the open procedure. As shown in Figure 2A, the cumulative incidence of recurrence among patients treated with the laparoscopic procedure did not differ significantly from that for patients who underwent open colectomy (two-sided P=0.32; hazard ratio for recurrence, 0.86; 95 percent confidence interval, 0.63 to 1.17). The estimated difference in the three-year recurrence-free rate was 2.4 percentage points in favor of the laparoscopic-surgery group (95 percent confidence interval, −2.9 to 7.8).

The overall survival rate was also very similar in the two groups (P=0.51; hazard ratio for death in the laparoscopic-surgery group, 0.91; 95 percent confidence interval, 0.68 to 1.21) (Fig. 3), as was the disease-free survival rate (117 events in the open-colectomy group and 118 events in the laparoscopic-surgery group; P=0.70 by the log-rank test; hazard ratio for recurrent disease in the laparoscopic-surgery group, 0.95; 95 percent confidence interval, 0.74 to 1.23). These findings held true for patients with any stage of cancer: there were no significant differences between treatment groups in the time to recurrence (Fig. 2), disease-free survival, or overall survival for any stage (Fig. 3). Conclusions drawn from the two sensitivity analyses (one conducted strictly according to the intention to treat and the other excluding patients with stage IV disease) were virtually identical (data not shown). The absence of a difference in the time to recurrence, disease-free survival, and overall survival persisted in multivariate analyses adjusted for the stratification factors. Tumor recurred in surgical wounds in three patients: two in the laparoscopic-surgery group (0.5 percent) and one in the open-colectomy group (0.2 percent, P=0.50).

DISCUSSION

This study was initiated in 1994 to ensure that laparoscopically assisted colectomy for colon cancer was properly tested before its use became widespread. Serious concern about the potential inadequacy of resection, possible staging inaccuracies, or the possibility that the use of a pneumoperitoneum altered the patterns of tumor dissemination demanded a prospective, randomized comparison. Surgeons fully supported the need for an evaluation of laparoscopically assisted colectomy for cancer, adopting a virtual moratorium on this practice outside of a clinical trial.[7,18] Our multi-institutional study provides data in support of the safety of laparoscopically assisted colectomy for colon cancer with respect to complications, time to recurrence, disease-free survival, and overall survival.

There has been little disagreement that the complications of laparoscopically assisted and open-colon resections are similar, because the critical steps of the procedures are essentially the same.[19,20] Our findings confirm that laparoscopically assist-

Table 2. Surgical, Pathological, and Postoperative Data.

Variable	Open Colectomy (N=428)	Laparoscopically Assisted Colectomy (N=435)	P Value
Length of incision — cm			<0.001
Median	18	6	
Range	3–35	2–35	
Duration of surgery — min			<0.001
Median	95	150	
Range	27–435	35–450	
Proximal margin — cm			0.38
Median	12	13	
Range	3–50	2–78	
Distal margin — cm			0.09
Median	11	10	
Range	1–42	2–40	
Conversion to open from laparoscopically assisted colectomy			—
No. (%)	—	90 (21)	
Reasons for conversion — no. (%)			
Not applicable	428 (100)	0	
Not converted	—	345 (79)	
Advanced disease	—	22 (5)	
Complicating disease	—	3 (1)	
Inadequate margins of resection	—	4 (1)	
No visualization of critical structures	—	12 (3)	
Unable to mobilize colon	—	10 (2)	
Adhesions	—	14 (3)	
Intraoperative complications	—	4 (1)	
Other	—	21 (5)	
Other organs resected — no. (%)*	62 (14)	33 (8)	0.001
Abdominal-wall adhesions — no. (%)	106 (25)	149 (34)	0.002
Bowel adhesions — no. (%)	58 (14)	95 (22)	0.001
Pelvic adhesions — no. (%)	59 (14)	66 (15)	0.53
Other types of intraabdominal disease — no. (%)	44 (10)	51 (12)	0.48
Duration of use of oral analgesics — days			0.02
Median	2	1	
Interquartile range	1–3	1–2	
Duration of use of parenteral narcotics — days			<0.001
Median	4	3	
Interquartile range	3–5	2–4	
Duration of hospitalization — days			<0.001
Median	6	5	
Interquartile range	5–7	4–6	
30-Day mortality — no. (%)	4 (1)	2 (<1)	0.40
Complications — no. (%)			
Overall	85 (20)	92 (21)	0.64
Intraoperative†	8 (2)	16 (4)	0.10
Postoperative (before discharge)	80 (19)	81 (19)	0.98
Grade of postoperative complications — no./total no. (%)			0.73
1	44/80 (55)	42/81 (52)	
2	33/80 (41)	34/81 (42)	
3	0/80	2/81 (2)	
4	3/80 (4)	3/81 (4)	

* Other organs resected included the gallbladder (10 patients in each group), gynecologic organs (24 in the open-colectomy group and 8 in the laparoscopic-surgery group), liver (9 and 1, respectively), the bladder and abdominal wall (6 and 3, respectively), small bowel (4 and 6, respectively), and other (9 and 5, respectively).

† Intraoperative complications included splenic injury (two in the open-colectomy group), bleeding (one in the open-colectomy group and eight in the laparoscopic-surgery group), bowel injury (two and six, respectively), and miscellaneous (three and two, respectively).

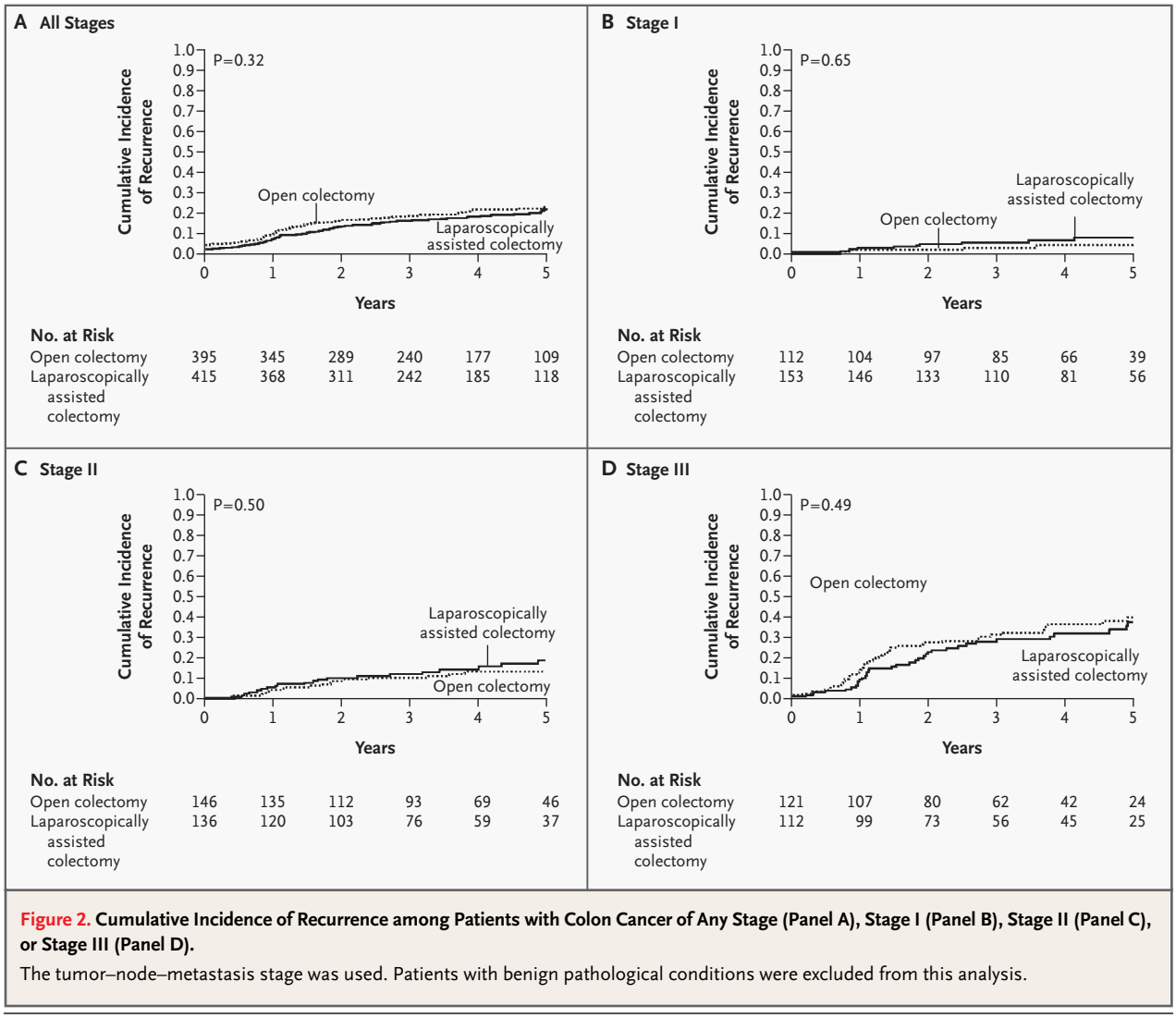

Figure 2. Cumulative Incidence of Recurrence among Patients with Colon Cancer of Any Stage (Panel A), Stage I (Panel B), Stage II (Panel C), or Stage III (Panel D).

The tumor–node–metastasis stage was used. Patients with benign pathological conditions were excluded from this analysis.

ed colectomy is not associated with a significant increase in overall complications.

In addition, other operative factors, including the extent of resection — specifically, the number of lymph nodes sampled, the length of bowel and mesentery resected, and the bowel margins — did not differ significantly between patients who underwent laparoscopically assisted surgery and those who underwent open colectomy. It will never be possible to determine whether laparoscopically assisted and open surgery provide the same degree of accuracy in terms of intraabdominal staging. Theoretically, laparoscopy may be inferior owing to the loss of tactile information provided by traditional surgical techniques. In practice, laparoscopy coupled with solid-organ imaging offers visual capabilities that seem to provide adequate staging information. The finding that the percentage of patients found to have metastatic disease at surgery did not differ significantly between groups provides indirect evidence of the adequacy of laparoscopic staging. Furthermore, there was no trend toward a higher rate of recurrence overall or among patients with stage III disease in the group treated laparoscopically, suggesting that the presence of undetected abdominal metastases is not an important limitation of the laparoscopic approach.

Our finding that laparoscopically assisted colectomy, as evaluated in our controlled setting, is safe for patients with colon cancer must be applied cau-

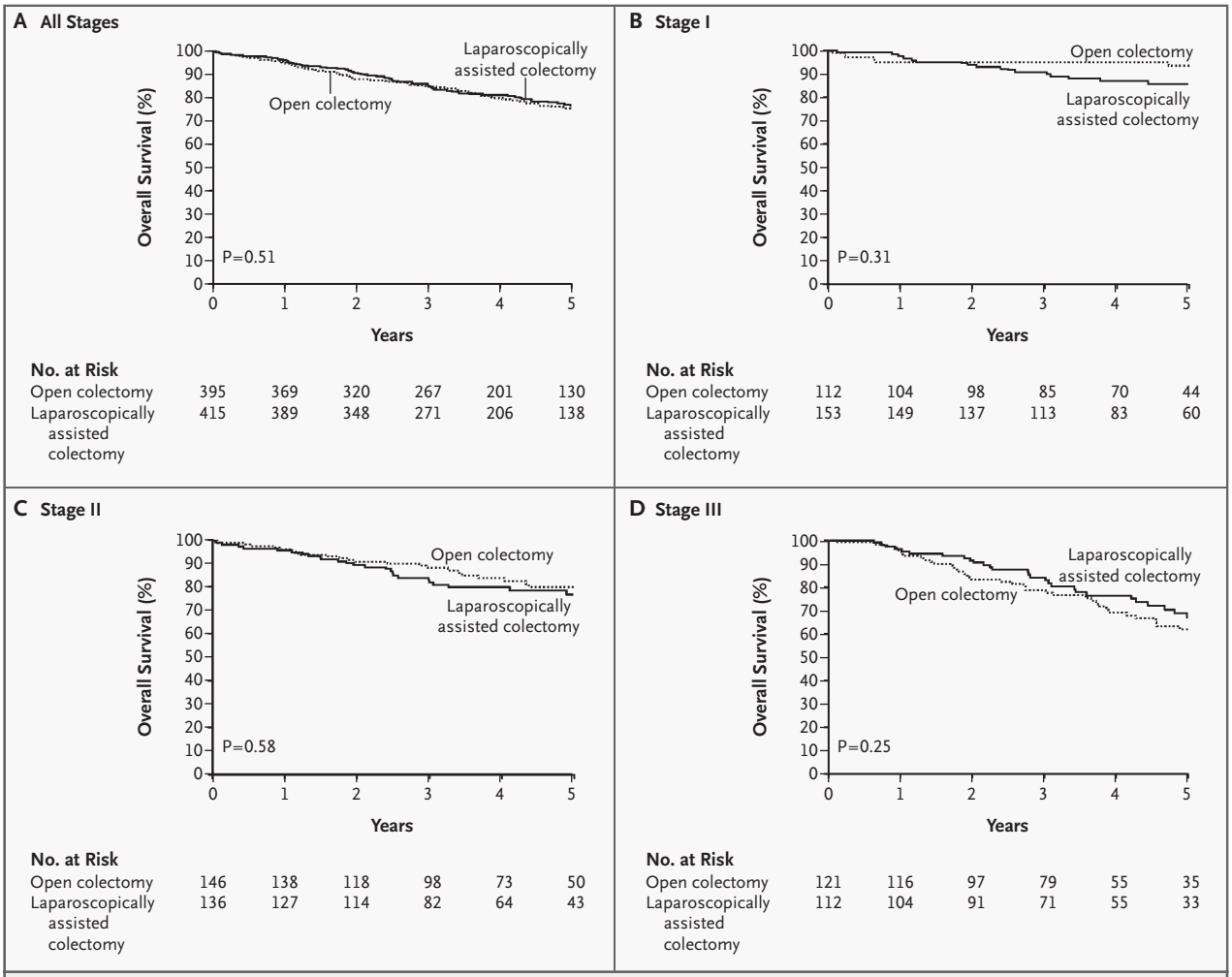

Figure 3. Overall Survival among Patients with Colon Cancer of Any Stage (Panel A), Stage I (Panel B), Stage II (Panel C), or Stage III (Panel D).
The tumor–node–metastasis stage was used. Patients with benign pathological conditions were excluded from this analysis.

tiously and selectively. To ensure patients' safety, we incorporated several precautions into our protocol. First, surgeon credentialing was required. Study surgeons had demonstrated laparoscopic experience, having performed at least 20 laparoscopically assisted colorectal operations. Second, surgeons demonstrated oncologic expertise; videotapes were scrutinized for the surgeons' oncologic techniques and practices. Third, patients with known locally advanced disease were not enrolled, and patients with intraoperative evidence of locally advanced disease underwent conversion to an open resection to ensure proper tumor management. The effect of these quality-control measures on the favorable outcomes cannot be accurately assessed. On the basis of this trial, adherence to these same standards in surgical practices should yield similar results.

The question of whether laparoscopically assisted colectomy should generally be offered to patients with cancer requires the synthesis of multiple factors. Our analysis of the total study population confirms the moderate benefits of laparoscopic surgery in terms of a decreased duration of hospitalization and decreased narcotic use that we previously described in the subgroup of patients evaluated for quality-of-life outcomes.[9] However, this finding must be balanced against the 21 percent rate of conversion to open colectomy as well as the increased operative times associated with the laparoscopic procedure. On the whole, these data suggest that

because laparoscopically assisted colectomy provides no additional risk of cancer, it is an acceptable alternative to open surgery for colon cancer.

The 21 percent rate of conversion from laparoscopically assisted to open surgery in this study is consistent with previously reported rates[10,19] and with the study design.[8] The detailed quality-of-life component of this trial suggests that greater benefits in terms of the quality of life and recovery may be possible if fewer procedures are converted.[9] Because no specific efforts were made to minimize conversion rates, these results may underestimate the results obtainable in an optimal practice. However, these results reflect current surgical practices. Participating surgeons had diverse training at practices throughout the United States and Canada. All passed rigorous protocol standards, and no data from the study suggested an influence of inexperience or a learning curve. Any decrease in conversion rates would therefore need to result from refining the process of patient selection, rather than from altering oncologic indications for conversion.

This study was not designed to test whether laparoscopically assisted colectomy is superior to open colectomy for cancer. Smaller clinical studies suggest that patients with cancer may benefit from laparoscopically assisted resection.[21] On the basis of data on the time to recurrence and survival, no advantage of laparoscopically assisted surgery was evident with respect to either all stages of cancer or high-risk subgroups.

Our findings suggest that it is safe to proceed with laparoscopically assisted colectomy in patients with cancer. Patients prefer to undergo minimally invasive procedures even if the benefits are limited, possibly because aesthetic results are considered to be better. The absence of oncologic risk and the resulting marginal short-term benefits counterbalance the longer operative times and provide support for plans to conduct comprehensive analyses of the quality of life, cost, and cost effectiveness of laparoscopically assisted colectomy.[8]

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APPENDIX

The members of the Clinical Outcomes of Surgical Therapy Study Group were as follows: Clinical Centers: *Mayo Clinic, Rochester, Minn.* — H. Nelson (North Central Cancer Treatment Group [NCCTG]), D. Sargent, T. Young-Fadok, G. Schroeder; *Washington University School of Medicine, St. Louis* — J. Fleshman (Radiation Therapy Oncology Group [RTOG]), E. Birnbaum; *St. Joseph's HealthCare, McMaster University, Hamilton, Ont., Canada* — M. Anvari (National Cancer Institute of Canada Clinical Trials Group [NCIC-CTG]), D. Birch; *Northwestern University, Feinberg School of Medicine, Chicago* — S.J. Stryker (Eastern Cooperative Oncology Group [ECOG], RTOG); *University of Southern California, Keck School of Medicine, Los Angeles* — R.W. Beart, Jr. (Southwest Oncology Group [SWOG]), A. Ortega; *University of Miami, Jackson Memorial Medical Center, Miami* — M. Hellinger (ECOG), R. Hartmann (ECOG), L. Sand; *St. Joseph Mercy Hospital, Ann Arbor, Mich.* — R. Flanagan, Jr. (NCCTG), R. Cleary (NCCTG); *Boone Hospital Center, Columbia, Mo.* — W. Peters (Cancer and Leukemia Group B [CALGB]); *Intermountain Health Care Cancer Services, LDS Hospital, Salt Lake City* — B. Christensen (RTOG); *Columbia Presbyterian Hospital, New York* — R. Whelan (SWOG); *University of Missouri, Columbia* — D. Ota (CALGB); *Midwest Surgical, P.A., Wichita, Kans.* — J. Hyder (SWOG); *Group Health Cooperative, Seattle* — D. Lauter (SWOG), E. Froines; *Lahey Clinic, Burlington, Mass.* — P. Marcello (CALGB); *M.D. Anderson Orlando Cancer Center, Orlando, Fla.* — S. Larach (RTOG), A. Ferrara; *Cleveland Clinic Florida, Weston* — S. Wexner (SWOG); *University of Texas Health Sciences Center, San Antonio* — J. Stauffer (SWOG); *University of Kentucky, Lexington* — A. Park (SWOG); *Lankenau Hospital Institute for Medical Research, Wynnewood, Pa.* — J. Marks (National Surgical Adjuvant Breast and Bowel Project [NSABP]); *Ottawa Regional Cancer Center, Ottawa, Ont.* — H. Stern (NCIC-CTG); *Creighton University, Omaha, Nebr.* — A. Thorson (NCCTG); *Lehigh Valley Hospital, Allentown, Pa.* — R. Boorse (ECOG); *Cleveland Clinic Foundation, Cleveland* — A. Senagore (SWOG), C. Delaney (SWOG); *St. Joseph Medical Center, Baltimore* — H.C. Kim (RTOG); *Norfolk Surgical Group, Eastern Virginia Medical School, Norfolk* — W.K. Ruffin (CALGB), G. Hoffman, G.W. Hubbard II, R. Gould, S. Wohlgemuth; *St. Luke's Hospital, Bethlehem, Pa.* — J. Lukaszczyk (ECOG), W.T. Reilly; *Mercy Health Center, Oklahoma City* — R.C. Thomas, Jr. (SWOG); *Mayo Clinic, Scottsdale, Ariz.* — R. Schlinkert (NCCTG); *Massachusetts General Hospital, Boston* — D. Rattner (CALGB); *Swedish Medical Center, Englewood, Colo.* — R. Bell (ECOG); *Centre Hospitalier Universitaire de Québec, Quebec City* — C. Thibault (NSABP); *East Carolina University, Brody School of Medicine, Greenville, N.C.* — W. Chapman III (NSABP); *Mount Sinai Hospital, New York* — B. Salky (CALGB), L.B. Katz; *Jefferson Regional Medical Center, Pittsburgh* — A. Fine (ECOG); *St. Joseph Mercy Hospital, Pontiac, Mich.* — A. Tootla (NCCTG); *Abington Memorial Hospital, Abington, Pa.* — R. Josloff (ECOG); *Brigham and Women's Hospital, Boston Medical Center, Boston* — R. Bleday (CALGB), R.A. Forse (CALGB); *Dartmouth–Hitchcock Medical Center, Lebanon, N.H.* — J. Sutton, Jr. (CALGB); *U.S. Air Force Wilford Hall Medical Center, Wilford Hall, Tex.* — T. Brown; *University of Virginia, Charlottesville* — B. Schirmer (ECOG); *Legacy Health System, Portland, Oreg.* — L. Swanstrom (SWOG); *Allegheny General Hospital, Pittsburgh* — D. Fowler (NSABP); *Mt. Diablo Medical Center, John Muir/Mt. Diablo Health System, Concord, Calif.* — S. Oommen (RTOG), H. Asbun (RTOG); *Huntington Memorial Hospital, Beverly Hills, Calif.* — E. Suddleson; *Kaiser Permanente Medical Center, San Diego, Calif.* — J. Greif (NSABP); *University of Massachusetts Memorial Medical Center, Worcester* — D. Litwin (CALGB); *University of Texas Southwestern Medical Center, Dallas* — C. Simmang (NSABP); Other participants: *Allegheny General Hospital, Pittsburgh* — T. Julian (NSABP), M. O'Connell (NSABP); *University of Pittsburgh, Pittsburgh* — H.S. Wieand (NSABP); *Dana–Farber Cancer Institute, Boston* — J. Weeks (CALGB).

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